WDR45 gene

WD repeat domain 45

Normal Function

The *WDR45* gene provides instructions for making a protein called WD40 repeat protein interacting with phosphoinositides 4 (WIPI4). WIPI4 is a member of a group of proteins each with a characteristic structure resembling a seven-bladed propeller. The WIPI4 protein is involved in the early stages of a process called autophagy, which helps clear unneeded materials from cells, including excess amounts of an iron storage protein called ferritin. In autophagy, worn-out cell parts (such as organelles, which are specialized structures that perform certain tasks within the cell) and other materials that are no longer needed are isolated in tiny compartments called autophagosomes. The WIPI4 protein helps control (regulate) the production and elongation of autophagosomes to contain the materials. The autophagosomes are then transported to organelles called lysosomes, which act as recycling centers within cells. Lysosomes use digestive enzymes to break down waste substances and recycle worn-out cell components.

Health Conditions Related to Genetic Changes

beta-propeller protein-associated neurodegeneration

More than 50 *WDR45* gene mutations have been identified in people with beta-propeller protein-associated neurodegeneration (BPAN), a disorder that damages the nervous system. This damage leads to delayed development and recurrent seizures (epilepsy) beginning in infancy or early childhood, movement problems that get worse over time, and a gradual loss of intellectual functioning in adulthood. Affected individuals eventually have a buildup of iron in the brain that can be seen with medical imaging; for this reason, BPAN is classified as a type of disorder called neurodegeneration with brain iron accumulation (NBIA).

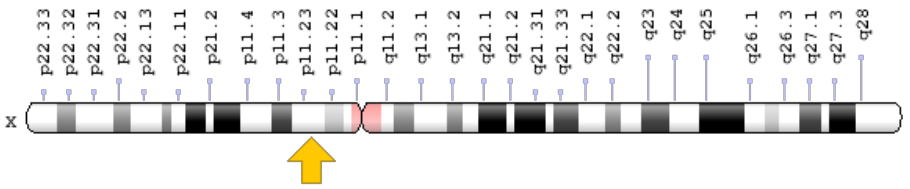
Most of the *WDR45* gene mutations identified in people with BPAN are thought to result in the production of an unstable WIPI4 protein that is quickly broken down, leading to loss of WIPI4 protein function. Without functional WIPI4 protein, the process of autophagy is impaired, making cells less efficient at removing damaged organelles and waste materials. Researchers suggest that nerve cells (neurons) may be particularly vulnerable to impaired autophagy because they have long extensions (axons and dendrites), making it even more difficult to transport the waste materials from these structures to the lysosomes in the cell body for recycling. The waste

materials can build up in these areas and damage them. Damage to neurons results in the neurological problems that occur in BPAN.

Chromosomal Location

Cytogenetic Location: Xp11.23, which is the short (p) arm of the X chromosome at position 11.23

Molecular Location: base pairs 49,074,433 to 49,101,121 on the X chromosome (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- JM5
- NBIA4
- NBIA5
- WD repeat-containing protein 45
- WD repeat domain phosphoinositide-interacting protein 4 isoform 1
- WD repeat domain phosphoinositide-interacting protein 4 isoform 2
- WD repeat domain, X-linked 1
- WD45 repeat protein interacting with phosphoinositides 4
- WDRX1
- WIPI-4
- WIPI4

Additional Information & Resources

Educational Resources

- Madame Curie Bioscience Database: Macroautophagy in Mammalian Cells https://www.ncbi.nlm.nih.gov/books/NBK6211/

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28WDR45%5BTIAB%5D%29+OR+%28WD+repeat+domain+45%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D

OMIM

- WD REPEAT-CONTAINING PROTEIN 45
  http://omim.org/entry/300526

Research Resources

- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=WDR45%5Bgene%5D
- HGNC Gene Family: WD repeat domain containing
  http://www.genenames.org/cgi-bin/genefamilies/set/362
- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=28912
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/11152
- UniProt
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https://ghr.nlm.nih.gov/gene/WDR45

Reviewed: May 2017
Published: June 27, 2017

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